(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 May 2005 (26.05.2005)

PCT

(10) International Publication Number
WO 2005/046637 A2

(51) International Patent Classification[7]: A61K 9/00

(21) International Application Number:
PCT/IB2004/003886

(22) International Filing Date:
11 November 2004 (11.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0326642.6 14 November 2003 (14.11.2003) GB
0326759.8 17 November 2003 (17.11.2003) GB

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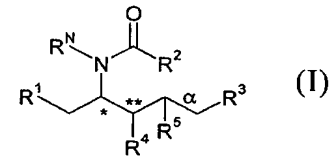
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,

[Continued on next page]

(54) Title: PHARMACEUTICAL FORMULATIONS EMPLOYING SHORT-CHAIN SPHINGOLIPIDS AND THEIR USE



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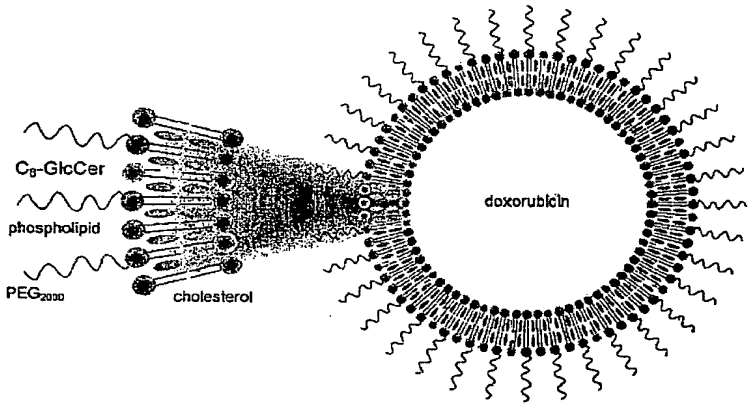

(57) Abstract: This invention pertains to pharmaceutical formulations which comprise (i) a drug (e.g., an amphiphilic drug) (e.g., an anthracycline) (e.g., doxorubicin) and (ii) a short-chain sphingolipid (e.g., a short-chain glycosphingolipid or a short-chain sphingomyelin) (e.g., N-octanoyl-glucosylceramide, referred to as C_8-GlcCer) (e.g., N-hexanoyl-sphingomyelin, referred to herein as C_6-SM), and which provide improved drug delivery and efficacy. The short-chain sphingolipidis selected from compounds of the following formula (I), wherein R^1 is independently: an O-linked saccharide group; or an O-linked polyhydric alcohol group; or: R^1 is independently: an O-linked (optionally N-(C_{1-4}alkyl)-substituted amino)-C_{1-6}alkyl-phosphate group; or an O-linked (polyhydric alcohol-substituted)C_{1-6}alkyl-phosphate group; R^2 is independently C_{3-9}alkyl, and is independently unsubstituted or substituted; R^3 is independently C_{7-19}alkyl, and is independently unsubstituted or substituted; R^4

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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

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is independently -H, -OH, or -O-C_{1-4}alkyl; R^N is independently -H or C_{1-4}alkyl; the bond marked with an alpha (α) is independently a single bond or a double bond; if the bond marked with an alpha (α) is a double bond, then R^5 is -H; if the bond marked with an alpha (α) is a single bond, then R^5 is -H or -OH; the carbon atom marked (*) is independently in an R-configuration or an S-configuration; the carbon atom marked (**) is independently in an R-configuration or an S-configuration; and pharmaceutically acceptable salts, solvates, esters, ethers, chemically protected forms thereof. In one embodiment, the pharmaceutical formulation is a liposomal pharmaceutical formulation prepared using a mixture of lipids comprising, at least, vesicle-forming lipids (e.g., phospholipids) (e.g., phosphatidylcholines) (e.g., fully hydrogenated soy phosphatidylcholine (HSPC)) (e.g., dipalmitoyl-phosphatidylcholine (DPPC)) and said short-chain sphingolipid, and optionally cholesterol and optionally a vesicle-forming lipid which is derivatized with a polymer chain (e.g., a phosphatidylethanolamine (PE) which is derivatized with polyethyleneglycol (PEG)) (e.g., N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG2000-DSPE). The present invention also pertains to methods for the preparation and use of such formulations.